

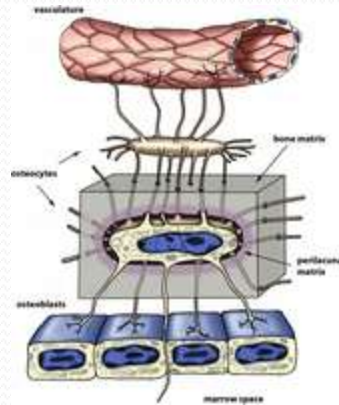
Bone as an Endocrine Organ

By

El Hadidy Mohamad El Hadidy
Prof Int Medicine & Endocrinology
Mansoura University

background

- Endocrine
- Paracrine
- autocrine



Classic endocrine glands

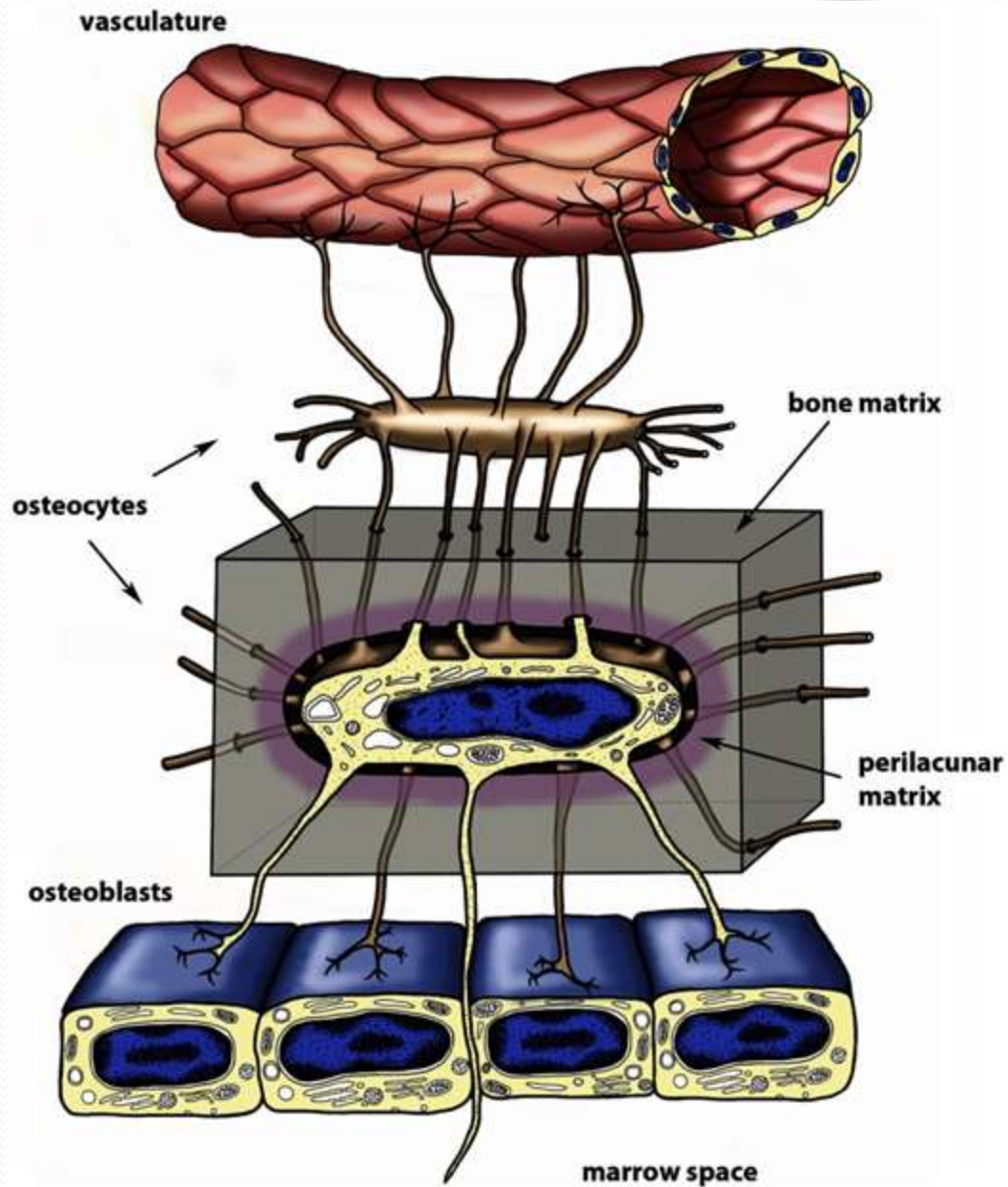
- Pituitary
- Thyroid
- parathyroid
- Adrenals
- gonads

Organs or tissues with endocrine functions:

- Fat cell: adiponectin
- Heart: ANP
- Kidney: erythropoietin
- Stomach: ghrelin
- Intestine: GLP 1
- Placenta: gonadotrophins
- Bone: FGF23, osteocalcin, sclerostin

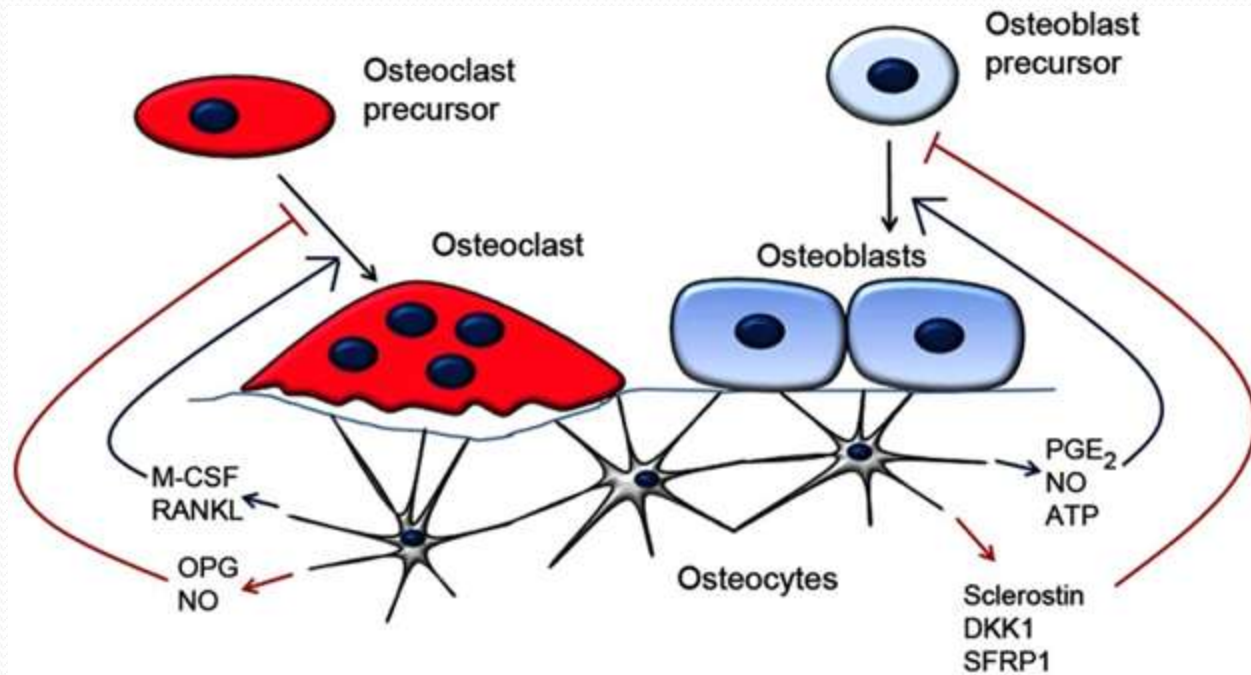
Bone cells

- Osteoblast: at surface of bone marrow
- Osteoclast: at surface of bone marrow
- Osteocyte: embedded within bone matrix, but connected to bone cells and BM with “lacunocanalicular system”



Endocrine function of bone

- FGF 23: secreted by osteocyte.
- Sclerostin: secreted by osteocyte.
- Osteocalcin: secreted by osteoblast.



FGF 23 and Klotho

- FGF 23 effect may direct effect or receptor mediated.
- FGF₂₃ receptor –mediated effect needs Klotho enzym.

Klotho

- Membrane bound: act as coreceptor, and dictates organ specificity of FGF23.
- Soluble Klotho (free in the circulation): regulate activity of cell surface proteins, and receptor for many tissues.

FGF23

(phosphatonin, phsphaturic H)

- *Kidney:*
 - inhibit renal tubular reabsorption of Pi, phsophaturia and hypophosphatemia.
 - Inhibit 1 alpha hydoroxyase: low active vitD, decrease of intestinal absorption of Ca,

FGF23

counter regulatory of vitD

- *Vitamin D:*

- inhibit activity of 1 alpha hydroxylase of the kidney.. Low active vit D.

- induce Cyp 24 in the kidney .. Increased 1,24 OH vit D... low active vit D.

FGF 23

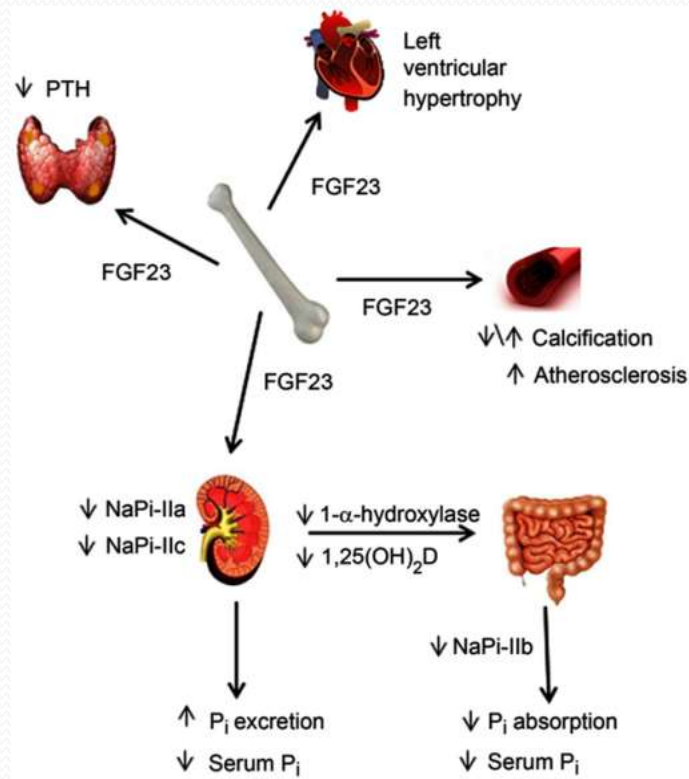
bone parathyroid axis

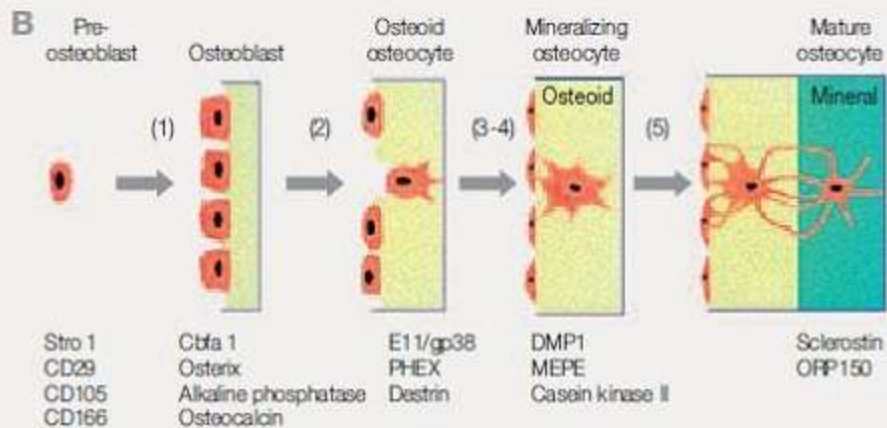
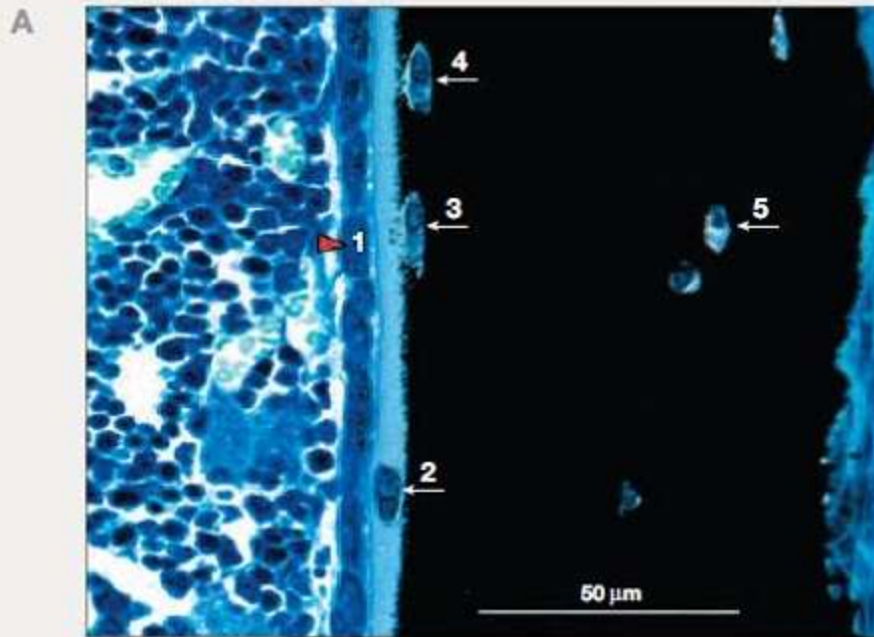
- Parathyroids:
inhibit release of PTH

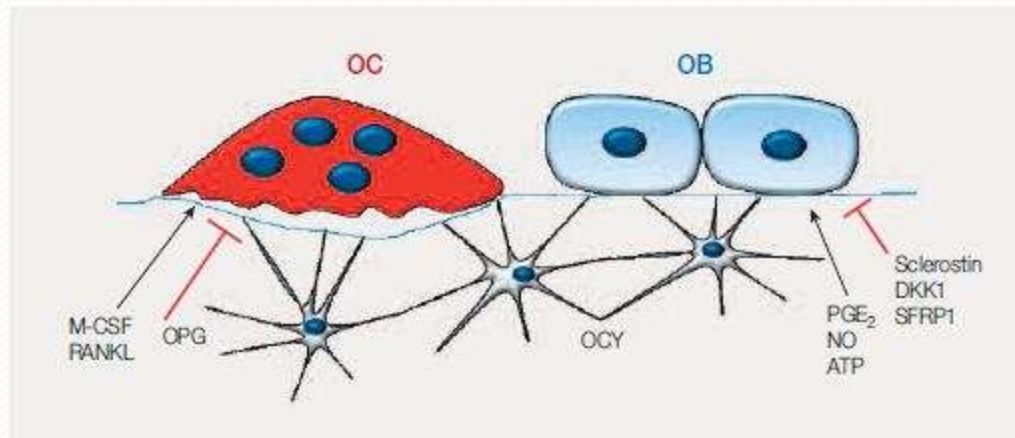
Intestine : low Ca & phosphate absorption through low
Vit D

FGF 23 and CVS

- Atherosclerosis with calcification of bl.vessels
 - LV: LV dysfunction, LVH, LV calcification, LV increased fat mass.
- Notably, these effects are Klotho-independent.







Osteocyte the mechanostat

- Mechanical loading ..induce osteoblastogenesis through release of factors by the osteocytes
eg. PGE₂, NO,

Muscle cell differentiation by soluble factors

- There is a cross talk between osteocyte and near by muscle cells through release of factors.

Sclerostin

(bone catabolic hormone)

- Secreted by the osteocyte
- Inhibit Wnt signalling pathway: decrease bone formation, decrease osteoblast differentiation, increase osteoblast apoptosis.

Sclerostin

- Measuring *sclerostin blood* Level in evaluation of many skeletal and non skeletal disorders.
- Early clinical trials using “ *sclerostin monoclonal antibodies*” revealed robust increase in bone density and prevent fracture. In the near future, it may be the best antiosteoporotic drug better than biphosphonate or teriparatide (Romosozumab).

Osteopontin

- Secreted by osteocyte.. Recruit mesenchymal stem cells.. Differentiate into osteoblast with alkaline phosphatase activity at the fracture site.

osteocalcin


- Secreted from the osteoblast.
- Measuring osteocalcin blood level reflect osteoblastic activity, measuring efficacy of drugs enhancing bone formation.

Osteocalcin, Endocrine function (bone and carbohydrate metabolism & male fertility)

- Pancreatic B cells: insulin secretion.
- Fat cell: adiponectin.
- Leydig cells of testicle interstitium: testosterone secretion

conclusion

- Bone endocrine function form an axis with Vit D and kidney to regulate calcium &phosphorus metabolism.
- Bone has a role in carbohydrate metabolism.
- Bone has a role in testosterone output.
- Bone has a role in CV health.



Thanks

.